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Crystal Structure of ClpA, an Hsp100 Chaperone and Regulator of ClpAP Protease

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Beamline(s): X9B

Introduction: *Escherichia coli* ClpA, an Hsp100/Clp chaperone and an integral component of the ATP-dependent ClpAP protease, participates in regulatory protein degradation and the dissolution and degradation of protein aggregates. ClpA consists of one N-terminal domain and two AAA^+ domains (ATPase associated with various cellular activities) and forms a hexamer in presence of ATP.

Methods and Materials: ClpA and its N-terminal domain were overexpressed, purified to homogeneity, and crystallized, respectively. The x-ray diffraction data of these protein crystals were collected. The crystal structures were solved by multiple isomorphous replacement.

Results: The crystal structure of the ClpA subunit reveals an N-terminal domain (N) with pseudo-twofold symmetry and two AAA^+ modules (D1 and D2) each consisting of a large and a small subdomain with ADP bound in the subdomain junction. The N-domain interacts with the D1 domain in a manner similar to adaptor-binding domains of other AAA^+ proteins. D1 and D2 domains are connected head-to-tail consistent with a cooperative and vectorial translocation of protein substrates. In a planar hexameric model of ClpA, built by assembling ClpA D1 and D2 into homohaxameric rings of known structures of AAA^+ modules, the differences in D1-D1 and D2-D2 interfaces correlate with their respective contributions to hexamer stability and ATPase activity.

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References:

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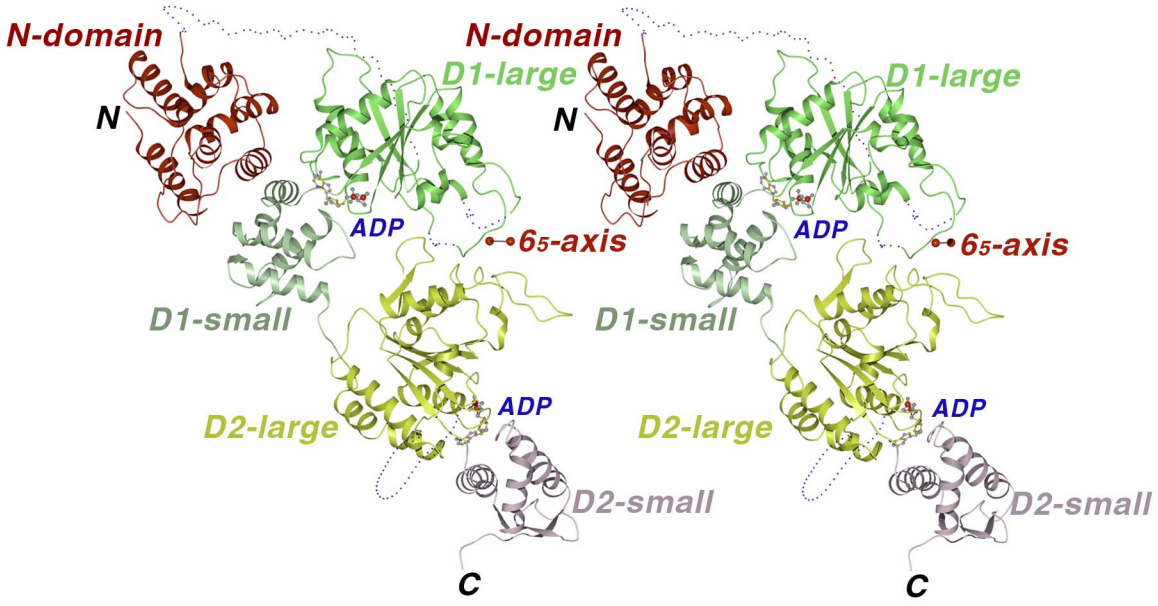

The ribbon diagram of structure of ClpA subunit.